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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/214,851	09/09/1999	EDWARD M SELLERS	064658.0129	8120
1059 7590 06/19/2007 BERESKIN AND PARR 40 KING STREET WEST BOX 401 TORONTO, ON M5H 3Y2 CANADA			EXAMINER JAGOE, DONNA A	
			ART UNIT 1614	PAPER NUMBER
			MAIL DATE 06/19/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 09/214,851	<b>Applicant(s)</b> SELLERS ET AL.	
	<b>Examiner</b> Donna Jagoe	<b>Art Unit</b> 1614	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 December 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 19,23,27,39-41 and 47-49 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 19,23,27,39-41 and 47-49 is/are rejected.
- 7) ☒ Claim(s) 47-49 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Applicants' arguments filed December 11, 2006 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

***Claims 19, 23, 27, 39-41 and 47-49 are pending in this application.***

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23 is rejected under 35 U.S.C. 102(b) as being anticipated by Vinals et al. U.S. Patent No. 3,977,418.

Vinals et al. teach a composition comprising nicotine and coumarin (a substance that inhibits CYP2A6), which would inherently regulate the metabolism of nicotine to cotinine. It is noted that the reference does not teach that the composition can be used in the manner instantly claimed, however, the intended use of the claimed composition does not patentably distinguish the composition, per se, since such undisclosed use is inherent in the reference composition. In order to be limiting, the intended use must

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create a structural difference between the claimed composition and the prior art composition. In the instant case, the intended use does not create a structural difference, thus the intended use is not limiting. Since the coumarin and nicotine are present in the composition of the patent, they are capable of performing the intended use of regulating metabolism of nicotine to cotinine, then it meets the claim.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

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under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 19, 27, 39-41 and 47-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over (U) Berkman et al. Biochemical Pharmacology, (1995) in view of (V) Seaton et al. Pharmac. Ther. 1993. and (W) Draper et al. Arch Biochem Biophys (1997) Berkman et al. teach that CYP2A6 is the primary enzyme that transforms (S)-nicotine to (S) nicotine  $\Delta^{1'5'}$ -iminium ion, which is converted to (S) cotinine by the action of an exogenously added aldehyde oxidase (page 565, column 2, 2<sup>nd</sup> paragraph bridging to page 566, first paragraph). The formation of (S)-cotinine is strongly dependent on the previous drug administration history of each subject, and among the highest rates for (S)-cotinine formation at low concentration correlated well with immunoreactivity for cytochrome P450 2A6 (see abstract). The in vitro/in vivo correlation of the results suggests that the low amount of (S)-nicotine N-1'-oxygenation and the large amount of (S)-cotinine formed in human smokers are determined primarily by the kinetic properties of the human monooxygenase enzyme systems. It doesn't teach that the CYP2A6 enzyme enhanced inhibition of nicotine metabolism. It teaches that in the presence of CYP2A6, lots of (S)-cotinine was formed. Seaton et al. teach that there are many variables to the metabolism of nicotine in a human. It teaches that Phenobarbital, an inducer of CYP450 enzymes induces not only metabolism of nicotine to cotinine, but also metabolism of cotinine to secondary metabolites (page 472 2<sup>nd</sup> paragraph).

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Conversely cimetidine, an agent that inhibits the CYP450 enzymes (page 472, 4<sup>th</sup> paragraph) decreased rates of nicotine metabolism so that twice as much nicotine was excreted unchanged in urine of Macaques (page 473 1<sup>st</sup> paragraph). Regarding the method for treatment of a condition requiring the regulation of nicotine metabolism to cotinine wherein the condition is dependent on tobacco use, Seaton et al. teach that chronic ethanol administration produces inductive effects of the CYP450 enzymes and induction of nicotine metabolism after chronic ethanol administration resulted in decreased plasma nicotine concentrations (increased metabolism) and might explain the increased urge to smoke cigarettes sometimes associated with heavy alcohol consumption. It would have been made obvious to one of ordinary skill in art at the time it was made to inhibit the CYP2A6 enzyme to inhibit metabolism of nicotine since Berkman et al. teach that CYP2A6 is the primary enzyme that transforms (S)-nicotine to (S) nicotine  $\Delta^{1'5'}$ -iminium ion, which is converted to (S)-cotinine. It does not teach the specific agents that inhibit the CYP2A6 enzymes, however, Draper et al. teach that inhibitors of CYP2A6 include clotrimazole, diethyldithiocarbamate, ellipticine, ketoconazole, 8-methoxypsoralen (methoxsalen), 4-methylpyrazole, metyrapone, miconazole, alpha naphthoflavone, nicotine p-nitrophenol and tranylcypromine (see abstract). Seaton et al. teaches inhibitors of CYP450 decrease nicotine metabolism (chronic ethanol administration) and agents that induce CYP450 increase nicotine metabolism (Phenobarbital). Combined with the teaching of Berkman et al. that CYP2A6 is the primary enzyme that transforms (S)-nicotine to (S) nicotine  $\Delta^{1'5'}$ -iminium

ion which is converted to (S) cotinine one would have been motivated to employ inhibitors of CYP2A6 to inhibit nicotine metabolism.

### ***New Claim Objections***

Claims 47-49 are objected to because of the following informalities: claims 47-49 are drawn to an imidazole antimycotic including *inter alia* pilocarpine. The claim is objected to because pilocarpine is not an imidazole antimycotic. Pilocarpine has no antifungal qualities, and it is not an imidazole. It is a parasymphomimetic, direct acting miotic. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its **ordinary** meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). Appropriate correction is required.

### ***Response to Arguments***

Applicant has amended claim 23 to include an inhibitor of CYP2B6, however, it is not clear what the difference is between the CYP2A6 inhibitors and the CYP2B6 inhibitors, consequently, the rejection of claim 23 is maintained. As a further note, Applicant asserts that claim 23 is objected to under 35 USC §102(b). To clarify, claim 23 is **rejected** under 35 USC § 102(b) (see office action dated September 11, 2006).

Applicant has amended claims 19 and 27 to include an inhibitor of CYP2B6, however, it is not clear what the difference is between the CYP2A6 inhibitors and the

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CYP2B6 inhibitors, consequently, the rejection of claims 19, 27, 39-41 and new claims 47-49 is maintained. As a further note, Applicant asserts that the claims are objected to under 35 USC §103(a). To clarify, claims 19, 27, 39-41 and 47-49 are **rejected** under 35 USC § 103(a) (see office action dated September 11, 2006).

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### ***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-

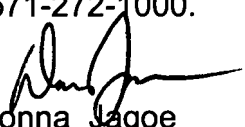


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0576. The examiner can normally be reached on Monday through Thursday from 9:00 A.M. - 3:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
Donna Jagoe  
Patent Examiner  
Art Unit 1614

May 21, 2007

  
ARDIN H. MARSCHEL  
SUPERVISORY PATENT EXAMINER